

THAT WHICH IS CLAIMED:

1. A method of treating a human subject for a cancer characterized by neoplastic B cell growth, said method comprising administering to said subject
5 combination antibody therapy, said therapy comprising administration of an effective amount of an anti-CD40 antibody or antigen-binding fragment thereof in combination with an anti-CD20 antibody or antigen-binding fragment thereof, wherein said anti-CD40 antibody or antigen-binding fragment thereof is free of significant agonist activity when bound to CD40 antigen, said anti-CD40 antibody or antigen-binding fragment thereof
10 being selected from the group consisting of:
- a) the monoclonal antibody CHIR-5.9 or CHIR-12.12;
 - b) the monoclonal antibody produced by the hybridoma cell line 5.9 or
12.12;
 - c) a monoclonal antibody comprising an amino acid sequence selected from
15 the group consisting of the sequence shown in SEQ ID NO:6, the sequence shown in SEQ ID NO:7, the sequence shown in SEQ ID NO:8, both the sequences shown in SEQ ID NO:6 and SEQ ID NO:7, and both the sequences shown in SEQ ID NO:6 and SEQ ID NO:8;
 - d) a monoclonal antibody comprising an amino acid sequence selected from
20 the group consisting of the sequence shown in SEQ ID NO:2, the sequence shown in SEQ ID NO:4, the sequence shown in SEQ ID NO:5, both the sequences shown in SEQ ID NO:2 and SEQ ID NO:4, and both the sequences shown in SEQ ID NO:2 and SEQ ID NO:5;
 - e) a monoclonal antibody having an amino acid sequence encoded by a
25 nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of the sequence shown in SEQ ID NO:1, the sequence shown in SEQ ID NO:3, and both the sequences shown in SEQ ID NO:1 and SEQ ID NO:3;
 - f) a monoclonal antibody that binds to an epitope capable of binding the monoclonal antibody produced by the hybridoma cell line 5.9 or 12.12;
 - 30 g) a monoclonal antibody that binds to an epitope comprising residues 82-87 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;

- h) a monoclonal antibody that binds to an epitope comprising residues 82-89 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;
- i) a monoclonal antibody that competes with the monoclonal antibody CHIR-5.9 or CHIR-12.12 in a competitive binding assay;
- 5 j) the monoclonal antibody of preceding item a) or a monoclonal antibody of any one of preceding items c)-i), wherein said antibody is recombinantly produced; and
- k) a monoclonal antibody that is an antigen-binding fragment of a monoclonal antibody of any one of preceding items a)-j), wherein said fragment retains the capability of specifically binding to said human CD40 antigen.

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2. The method of claim 1, wherein said combination antibody therapy provides a synergistic therapeutic effect.

3. The method of claim 1, wherein said antigen-binding fragment of said anti-CD40 antibody or said anti-CD20 antibody is selected from the group consisting of a Fab fragment, an F(ab')₂ fragment, an Fv fragment, and a single-chain Fv fragment.

4. The method of claim 1, wherein said anti-CD20 antibody is selected from the group consisting of a human anti-CD20 antibody, a murine anti-CD20 antibody, a chimeric anti-CD20 antibody, and a humanized anti-CD20 antibody.

5. The method of claim 4, wherein said anti-CD20 antibody is IDEC-C2B8 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

6. The method of claim 5, wherein said anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.

7. The method of claim 1, wherein the cancer is selected from the group consisting of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, multiple myeloma, B cell lymphoma, high-grade B cell lymphoma, intermediate-grade B cell lymphoma, low-grade B cell lymphoma, B cell acute lymphoblastic leukemia,

myeloblastic leukemia, Hodgkin's disease, plasmacytoma, follicular lymphoma, follicular small cleaved lymphoma, follicular large cell lymphoma, follicular mixed small cleaved lymphoma, diffuse small cleaved cell lymphoma, diffuse small lymphocytic lymphoma, prolymphocytic leukemia, lymphoplasmacytic lymphoma, marginal zone lymphoma, mucosal associated lymphoid tissue lymphoma, monocytoid B cell lymphoma, splenic lymphoma, hairy cell leukemia, diffuse large cell lymphoma, mediastinal large B cell lymphoma, lymphomatoid granulomatosis, intravascular lymphomatosis, diffuse mixed cell lymphoma, diffuse large cell lymphoma, immunoblastic lymphoma, Burkitt's lymphoma, AIDS-related lymphoma, and mantle cell lymphoma.

8. The method of claim 1, wherein said anti-CD20 antibody or antigen-binding fragment thereof and said antagonist anti-CD40 antibody or antigen-binding fragment thereof are administered sequentially.

9. The method of claim 1, wherein said anti-CD20 antibody or antigen-binding fragment thereof and said antagonist anti-CD40 antibody or antigen-binding fragment thereof are administered simultaneously.

10. A method of treating a human subject for a cancer that is characterized by neoplastic B cell growth and which is refractory to treatment with an anti-CD20 antibody or antigen-binding fragment thereof, said method comprising administering to said subject combination antibody therapy, wherein said therapy comprises administration of an effective amount of an anti-CD40 antibody or antigen-binding fragment thereof in combination with said anti-CD20 antibody or antigen-binding fragment thereof, wherein said anti-CD40 antibody or antigen-binding fragment thereof is free of significant agonist activity when bound to CD40 antigen, said anti-CD40 antibody or antigen-binding fragment thereof being selected from the group consisting of:

a) the monoclonal antibody CHIR-5.9 or CHIR-12.12;

b) the monoclonal antibody produced by the hybridoma cell line 5.9 or 12.12;

c) a monoclonal antibody comprising an amino acid sequence selected from the group consisting of the sequence shown in SEQ ID NO:6, the sequence shown in SEQ ID NO:7, the sequence shown in SEQ ID NO:8, both the sequences shown in SEQ ID NO:6 and SEQ ID NO:7, and both the sequences shown in SEQ ID NO:6 and SEQ ID NO:8;

d) a monoclonal antibody comprising an amino acid sequence selected from the group consisting of the sequence shown in SEQ ID NO:2, the sequence shown in SEQ ID NO:4, the sequence shown in SEQ ID NO:5, both the sequences shown in SEQ ID NO:2 and SEQ ID NO:4, and both the sequences shown in SEQ ID NO:2 and SEQ ID NO:5;

e) a monoclonal antibody having an amino acid sequence encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of the sequence shown in SEQ ID NO:1, the sequence shown in SEQ ID NO:3, and both the sequences shown in SEQ ID NO:1 and SEQ ID NO:3;

f) a monoclonal antibody that binds to an epitope capable of binding the monoclonal antibody produced by the hybridoma cell line 5.9 or 12.12;

g) a monoclonal antibody that binds to an epitope comprising residues 82-87 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;

h) a monoclonal antibody that binds to an epitope comprising residues 82-89 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;

i) a monoclonal antibody that competes with the monoclonal antibody CHIR-5.9 or CHIR-12.12 in a competitive binding assay;

j) the monoclonal antibody of preceding item a) or a monoclonal antibody of any one of preceding items c)-i), wherein said antibody is recombinantly produced; and

k) a monoclonal antibody that is an antigen-binding fragment of a monoclonal antibody of any one of preceding items a)-j), wherein said fragment retains the capability of specifically binding to said human CD40 antigen.

11. The method of claim 10, wherein said combination antibody therapy provides a synergistic therapeutic effect.

12. The method of claim 10, wherein said antigen-binding fragment of said anti-CD40 antibody or said anti-CD20 antibody is selected from the group consisting of a Fab fragment, an F(ab')₂ fragment, an Fv fragment, and a single-chain Fv fragment.

5 13. The method of claim 10, wherein said anti-CD20 antibody is selected from the group consisting of a human anti-CD20 antibody, a murine anti-CD20 antibody, a chimeric anti-CD20 antibody, and a humanized anti-CD20 antibody.

10 14. The method of claim 13, wherein said anti-CD20 antibody is IDEC-C2B8 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

15 15. The method of claim 14, wherein said anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.

15 16. The method of claim 10, wherein the cancer is selected from the group consisting of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, multiple myeloma, B cell lymphoma, high-grade B cell lymphoma, intermediate-grade B cell lymphoma, low-grade B cell lymphoma, B cell acute lymphoblastic leukemia, myeloblastic leukemia, Hodgkin's disease, plasmacytoma, follicular lymphoma, 20 follicular small cleaved lymphoma, follicular large cell lymphoma, follicular mixed small cleaved lymphoma, diffuse small cleaved cell lymphoma, diffuse small lymphocytic lymphoma, prolymphocytic leukemia, lymphoplasmacytic lymphoma, marginal zone lymphoma, mucosal associated lymphoid tissue lymphoma, monocytoid B cell lymphoma, splenic lymphoma, hairy cell leukemia, diffuse large cell lymphoma, 25 mediastinal large B cell lymphoma, lymphomatoid granulomatosis, intravascular lymphomatosis, diffuse mixed cell lymphoma, diffuse large cell lymphoma, immunoblastic lymphoma, Burkitt's lymphoma, AIDS-related lymphoma, and mantle cell lymphoma.

17. The method of claim 10, wherein said anti-CD20 antibody or antigen-binding fragment thereof and said antagonist anti-CD40 antibody or antigen-binding fragment thereof are administered sequentially.

5 18. The method of claim 10, wherein said anti-CD20 antibody or antigen-binding fragment thereof and said antagonist anti-CD40 antibody or antigen-binding fragment thereof are administered simultaneously.

10 19. A method for inhibiting growth of a tumor comprising neoplastic B cells, comprising contacting said cells with an effective amount of an anti-CD40 antibody or antigen binding fragment thereof in combination with an anti-CD20 antibody or antigen binding fragment thereof, wherein said anti-CD40 antibody or antigen-binding fragment thereof is free of significant agonist activity when bound to CD40 antigen, said anti-CD40 antibody or antigen-antigen binding fragment thereof being selected from the
15 group consisting of:

a) the monoclonal antibody CHIR-5.9 or CHIR-12.12;

b) the monoclonal antibody produced by the hybridoma cell line 5.9 or 12.12;

c) a monoclonal antibody comprising an amino acid sequence selected from
20 the group consisting of the sequence shown in SEQ ID NO:6, the sequence shown in SEQ ID NO:7, the sequence shown in SEQ ID NO:8, both the sequence shown in SEQ ID NO:6 and SEQ ID NO:7, and both the sequence shown in SEQ ID NO:6 and SEQ ID NO:8;

d) a monoclonal antibody comprising an amino acid sequence selected from
25 the group consisting of the sequence shown in SEQ ID NO:2, the sequence shown in SEQ ID NO:4, the sequence shown in SEQ ID NO:5, both the sequence shown in SEQ ID NO:2 and SEQ ID NO:4, and both the sequence shown in SEQ ID NO:2 and SEQ ID NO:5;

e) a monoclonal antibody having an amino acid sequence encoded by a
30 nucleic acid molecule comprising a nucleotide sequence selected from the group

consisting of the sequence shown in SEQ ID NO:1, the sequence shown in SEQ ID NO:3, and both the sequence shown in SEQ ID NO:1 and SEQ ID NO:3;

f) a monoclonal antibody that binds to an epitope capable of binding the monoclonal antibody produced by the hybridoma cell line 5.9 or 12.12;

5 g) a monoclonal antibody that binds to an epitope comprising residues 82-87 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;

h) a monoclonal antibody that binds to an epitope comprising residues 82-89 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;

i) a monoclonal antibody that competes with the monoclonal antibody
10 CHIR-5.9 or CHIR-12.12 in a competitive binding assay;

j) the monoclonal antibody of preceding item a) or a monoclonal antibody of any one of preceding items c)-i), wherein said antibody is recombinantly produced; and

k) a monoclonal antibody that is an antigen-binding fragment of a monoclonal antibody of any one of preceding items a)-j), wherein said fragment retains
15 the capability of specifically binding to said human CD40 antigen.

20. The method of claim 19, wherein growth of said tumor is synergistically inhibited.

20 21. The method of claim 19, wherein said antigen-binding fragment of said anti-CD40 antibody or said anti-CD20 antibody is selected from the group consisting of a Fab fragment, an F(ab')₂ fragment, an Fv fragment, and a single-chain Fv fragment.

22. The method of claim 19, wherein said anti-CD20 antibody is selected from
25 the group consisting of a human anti-CD20 antibody, a murine anti-CD20 antibody, a chimeric anti-CD20 antibody, and a humanized anti-CD20 antibody.

23. The method of claim 22, wherein said anti-CD20 antibody is IDEC-C2B8 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

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24. The method of claim 23, wherein said anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.

25. The method of claim 19, wherein said tumor is associated with a cancer
5 selected from the group consisting of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, multiple myeloma, B cell lymphoma, high-grade B cell lymphoma, intermediate-grade B cell lymphoma, low-grade B cell lymphoma, B cell acute lymphoblastic leukemia, myeloblastic leukemia, Hodgkin's disease, plasmacytoma, follicular lymphoma, follicular small cleaved lymphoma, follicular large cell lymphoma,
10 follicular mixed small cleaved lymphoma, diffuse small cleaved cell lymphoma, diffuse small lymphocytic lymphoma, prolymphocytic leukemia, lymphoplasmacytic lymphoma, marginal zone lymphoma, mucosal associated lymphoid tissue lymphoma, monocytoid B cell lymphoma, splenic lymphoma, hairy cell leukemia, diffuse large cell lymphoma, mediastinal large B cell lymphoma, lymphomatoid granulomatosis, intravascular
15 lymphomatosis, diffuse mixed cell lymphoma, diffuse large cell lymphoma, immunoblastic lymphoma, Burkitt's lymphoma, AIDS-related lymphoma, and mantle cell lymphoma.

26. The method of claim 25, wherein said cancer is refractory to treatment
20 with said anti-CD20 antibody or antigen-binding fragment thereof.

27. The method of claim 26, wherein said anti-CD20 antibody is IDEC-C2B8 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

28. The method of claim 27, wherein said anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.

29. A method of treating a human subject for a cancer characterized by neoplastic B cell growth, said method comprising administering to said subject
30 combination antibody therapy, said therapy comprising administration of an effective amount of an antagonist anti-CD40 antibody or antigen-binding fragment thereof in

combination with an anti-CD20 antibody or antigen-binding fragment thereof, wherein said antagonist anti-CD40 antibody or antigen-binding fragment thereof specifically binds Domain 2 of human CD40 antigen and is free of significant agonist activity when bound to Domain 2 of human CD40 antigen.

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30. The method of claim 29, wherein said combination antibody therapy provides a synergistic therapeutic effect.

31. The method of claim 29, wherein said antagonist anti-CD40 antibody is a human antibody.

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32. The method of claim 29, wherein said antagonist anti-CD40 antibody is recombinantly produced.

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33. The method of claim 29, wherein said antagonist anti-CD40 antibody has the binding specificity of an antibody selected from the group consisting of the antibody produced by hybridoma cell line 5.9 and the antibody produced by hybridoma cell line 12.12.

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34. The method of claim 29, wherein said antagonist anti-CD40 antibody is selected from the group consisting of the antibody produced by the hybridoma cell line deposited with the ATCC as Patent Deposit No. PTA-5542 and the antibody produced by the hybridoma cell line deposited with the ATCC as Patent Deposit No. PTA-5543.

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35. The method of claim 29, wherein said antagonist anti-CD40 antibody has the binding specificity of monoclonal antibody CHIR-12.12 or CHIR-5.9.

36. The method of claim 29, wherein said antagonist anti-CD40 antibody binds to an epitope comprising residues 82-87 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12.

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37. The method of claim 29, wherein said antagonist anti-CD40 antibody or antigen-binding fragment thereof is selected from the group consisting of:

a) a monoclonal antibody comprising an amino acid sequence selected from the group consisting of the sequence shown in SEQ ID NO:2, the sequence shown in SEQ ID NO:4, the sequence shown in SEQ ID NO:5, both the sequence shown in SEQ ID NO:2 and SEQ ID NO:4, and both the sequence shown in SEQ ID NO:2 and SEQ ID NO:5;

b) a monoclonal antibody having an amino acid sequence encoded by a nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of the sequence shown in SEQ ID NO:1, the sequence shown in SEQ ID NO:3, and both the sequence shown in SEQ ID NO:1 and SEQ ID NO:3;

c) a monoclonal antibody that binds to an epitope capable of binding the monoclonal antibody produced by the hybridoma cell line 12.12;

d) a monoclonal antibody that binds to an epitope comprising residues 82-87 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;

e) a monoclonal antibody that competes with the monoclonal antibody CHIR-12.12 in a competitive binding assay;

f) a monoclonal antibody of any one of preceding items a)-e), wherein said antibody is recombinantly produced; and

g) a monoclonal antibody that is an antigen-binding fragment of the CHIR-12.12 monoclonal antibody or an antigen-binding fragment of a monoclonal antibody of any one of preceding items a)-f), where the fragment retains the capability of specifically binding to said human CD40 antigen.

38. The method of claim 29, wherein said antigen-binding fragment of said antagonist anti-CD40 antibody or said anti-CD20 antibody is selected from the group consisting of a Fab fragment, an F(ab')₂ fragment, an Fv fragment, and a single-chain Fv fragment.

39. The method of claim 29, wherein said anti-CD20 antibody is selected from the group consisting of a human anti-CD20 antibody, a murine anti-CD20 antibody, a chimeric anti-CD20 antibody, and a humanized anti-CD20 antibody.

5 40. The method of claim 39, wherein said anti-CD20 antibody is IDEC-C2B8 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

41. The method of claim 40, wherein said antagonist anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.

10 42. The method of claim 29, wherein said cancer is selected from the group consisting of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, multiple myeloma, B cell lymphoma, high-grade B cell lymphoma, intermediate-grade B cell lymphoma, low-grade B cell lymphoma, B cell acute lymphoblastic leukemia,
15 myeloblastic leukemia, Hodgkin's disease, plasmacytoma, follicular lymphoma, follicular small cleaved lymphoma, follicular large cell lymphoma, follicular mixed small cleaved lymphoma, diffuse small cleaved cell lymphoma, diffuse small lymphocytic lymphoma, prolymphocytic leukemia, lymphoplasmacytic lymphoma, marginal zone lymphoma, mucosal associated lymphoid tissue lymphoma, monocytoid B cell
20 lymphoma, splenic lymphoma, hairy cell leukemia, diffuse large cell lymphoma, mediastinal large B cell lymphoma, lymphomatoid granulomatosis, intravascular lymphomatosis, diffuse mixed cell lymphoma, diffuse large cell lymphoma, immunoblastic lymphoma, Burkitt's lymphoma, AIDS-related lymphoma, and mantle cell lymphoma.

25 43. The method of claim 42, wherein said cancer is refractory to treatment with said anti-CD20 antibody or antigen-binding fragment thereof.

44. The method of claim 43, wherein said anti-CD20 antibody is IDEC-C2B8
30 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

45. The method of claim 44, wherein said antagonist anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.

46. The method of claim 29, wherein said anti-CD20 antibody or antigen-binding fragment thereof and said antagonist anti-CD40 antibody or antigen-binding fragment thereof are administered sequentially.

47. The method of claim 29, wherein said anti-CD20 antibody or antigen-binding fragment thereof and said antagonist anti-CD40 antibody or antigen-binding fragment thereof are administered simultaneously.

48. A method for inhibiting growth of a tumor comprising neoplastic B cells, comprising contacting said cells with an effective amount of an antagonist anti-CD40 antibody or antigen binding fragment thereof in combination with an anti-CD20 antibody or antigen binding fragment thereof, wherein said antagonist anti-CD40 antibody or antigen-binding fragment thereof specifically binds Domain 2 of human CD40 antigen and is free of significant agonist activity when bound to Domain 2 of human CD40 antigen.

49. The method of claim 48, wherein growth of said tumor is synergistically inhibited.

50. The method of claim 48, wherein said antagonist anti-CD40 antibody is a human antibody.

51. The method of claim 48, wherein said antagonist anti-CD40 antibody is recombinantly produced.

52. The method of claim 48, wherein said antagonist anti-CD40 antibody has the binding specificity of an antibody selected from the group consisting of the antibody

produced by hybridoma cell line 5.9 and the antibody produced by hybridoma cell line 12.12.

53. The method of claim 48, wherein said antagonist anti-CD40 antibody is
5 selected from the group consisting of the antibody produced by the hybridoma cell line deposited with the ATCC as Patent Deposit No. PTA-5542 and the antibody produced by the hybridoma cell line deposited with the ATCC as Patent Deposit No. PTA-5543.

54. The method of claim 48, wherein said antagonist anti-CD40 antibody has
10 the binding specificity of monoclonal antibody CHIR-12.12 or CHIR-5.9.

55. The method of claim 48, wherein said antagonist anti-CD40 antibody
binds to an epitope comprising residues 82-87 of the human CD40 sequence shown in
SEQ ID NO:10 or SEQ ID NO:12.

56. The method of claim 48, wherein said antagonist anti-CD40 antibody or
antigen-binding fragment thereof is selected from the group consisting of:

a) a monoclonal antibody comprising an amino acid sequence selected from
the group consisting of the sequence shown in SEQ ID NO:2, the sequence shown in
20 SEQ ID NO:4, the sequence shown in SEQ ID NO:5, both the sequence shown in SEQ
ID NO:2 and SEQ ID NO:4, and both the sequence shown in SEQ ID NO:2 and SEQ ID
NO:5;

b) a monoclonal antibody having an amino acid sequence encoded by a
nucleic acid molecule comprising a nucleotide sequence selected from the group
25 consisting of the sequence shown in SEQ ID NO:1, the sequence shown in SEQ ID
NO:3, and both the sequence shown in SEQ ID NO:1 and SEQ ID NO:3;

c) a monoclonal antibody that binds to an epitope capable of binding the
monoclonal antibody produced by the hybridoma cell line 12.12;

d) a monoclonal antibody that binds to an epitope comprising residues 82-87
30 of the human CD40 sequence shown in SEQ ID NO:10 or SEQ ID NO:12;

e) a monoclonal antibody that competes with the monoclonal antibody CHIR-12.12 in a competitive binding assay;

f) a monoclonal antibody of any one of preceding items a)-e), wherein said antibody is recombinantly produced; and

5 g) a monoclonal antibody that is an antigen-binding fragment of the CHIR-12.12 monoclonal antibody or an antigen-binding fragment of a monoclonal antibody of any one of preceding items a)-f), where the fragment retains the capability of specifically binding to said human CD40 antigen.

10 57. The method of claim 48, wherein said antigen-binding fragment of said antagonist anti-CD40 antibody or said anti-CD20 antibody is selected from the group consisting of a Fab fragment, an F(ab')₂ fragment, an Fv fragment, and a single-chain Fv fragment.

15 58. The method of claim 48, wherein said anti-CD20 antibody is selected from the group consisting of a human anti-CD20 antibody, a murine anti-CD20 antibody, a chimeric anti-CD20 antibody, and a humanized anti-CD20 antibody.

20 59. The method of claim 58, wherein said anti-CD20 antibody is IDEC-C2B8 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

60. The method of claim 59, wherein said anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.

25 61. The method of claim 48, wherein said cancer is selected from the group consisting of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, multiple myeloma, B cell lymphoma, high-grade B cell lymphoma, intermediate-grade B cell lymphoma, low-grade B cell lymphoma, B cell acute lymphoblastic leukemia, myeloblastic leukemia, Hodgkin's disease, plasmacytoma, follicular lymphoma,
30 follicular small cleaved lymphoma, follicular large cell lymphoma, follicular mixed small cleaved lymphoma, diffuse small cleaved cell lymphoma, diffuse small lymphocytic

lymphoma, prolymphocytic leukemia, lymphoplasmacytic lymphoma, marginal zone lymphoma, mucosal associated lymphoid tissue lymphoma, monocytoid B cell lymphoma, splenic lymphoma, hairy cell leukemia, diffuse large cell lymphoma, mediastinal large B cell lymphoma, lymphomatoid granulomatosis, intravascular lymphomatosis, diffuse mixed cell lymphoma, diffuse large cell lymphoma, immunoblastic lymphoma, Burkitt's lymphoma, AIDS-related lymphoma, and mantle cell lymphoma.

62. The method of claim 61, wherein said cancer is refractory to treatment with said anti-CD20 antibody or antigen-binding fragment thereof.

63. The method of claim 62, wherein said anti-CD20 antibody is IDEC-C2B8 or an anti-CD20 antibody having the binding characteristics of IDEC-C2B8.

64. The method of claim 63, wherein said anti-CD40 antibody is the monoclonal antibody CHIR-5.9 or CHIR-12.12.